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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/847,670	05/02/2001	Barry C. Finzel	6263.N	4815
26813	7590	06/14/2004	EXAMINER	
MUETING, RAASCH & GEBHARDT, P.A. P.O. BOX 581415 MINNEAPOLIS, MN 55458			SMITH, CAROLYN L	
			ART UNIT	PAPER NUMBER

1631

DATE MAILED: 06/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/847,670

Applicant(s)

FINZEL ET AL.

Examiner

Carolyn L Smith

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 March 2004 and 08 April 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 31,35,38-43 and 47-61 is/are pending in the application.
- 4a) Of the above claim(s) 31,35,47 and 48 is/are withdrawn from consideration.
- 5) ☒ Claim(s) 38-41 and 43 is/are allowed.
- 6) ☒ Claim(s) 42 and 49-61 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☒ Claim(s) 31,35,38-43 and 47-61 are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input checked="" type="checkbox"/> Other: <u>Republication granted</u> . |

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submissions, filed 3/9/04 and 4/8/04, have been entered. Amended claims 42, 43, 49-52, and 58-59 as well as new claims 60-61, filed 3/9/04, are acknowledged.

Applicants' arguments, filed 3/9/04, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

The request for republishing, filed 10/16/03, has been granted.

Claims 38-43 and 49-61 are herein under examination.

Specification

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The present title is directed to crystals, crystallographic structure, and methods whereas in contrast the elected claims do not contain methods. Once product claims become allowable, the practice of rejoinder regarding

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method claims is acknowledged. At that time it would be appropriate to add "methods" into the title of the claimed invention.

Claims Rejected Under 35 USC § 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in *Ex parte Forman*, 230 USPQ 546 (BPAI 1986) and reiterated by the Court of Appeals in *In re Wands*, 8 USPQ2d 1400 at 1404 (CAFC 1988). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. The Board also stated that although the level of the skill in molecular biology is high, the results of experiments in genetic engineering are unpredictable. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

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LACK OF ENABLEMENT

Claims 42 and 49-61 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the claimed invention.

Although Applicants have disclosed information to enable one skilled in the art to make the tetragonal and orthorhombic crystals of crystalline Hepatitis C virus helicase with unit cell dimensions $a = b = 109 \text{ \AA} \pm 3 \text{ \AA}$; $c = 84 \text{ \AA} \pm 2 \text{ \AA}$; $\alpha = \beta = \gamma = 90^\circ$; and space group $P4_1$ as well as $a = 66 \text{ \AA} \pm 2 \text{ \AA}$; $b = 110 \text{ \AA} \pm 3 \text{ \AA}$; $c = 64 \text{ \AA} \pm 2 \text{ \AA}$; $\alpha = \beta = \gamma = 90^\circ$; and space group $P2_12_12_1$, respectively, the specification does not reasonably provide enablement for other crystalline Hepatitis C virus helicases and compositions comprising the same as stated in claims 42, 49-61. The claims are broader than the enablement provided by the disclosure with regard to the large number of possible crystalline helicases that could be made. As the science of protein crystallization is well known to be a trial and error procedure with unpredictable results (Drenth, page 1, lines 13-20), one skilled in the art would require clear and precise guidance to make any particular crystal. This unpredictability includes making a unit cell crystal when there is no tetragonal or orthorhombic characteristic also produced, as encompassed in instant claims 53-57. Accordingly, it would be very difficult for a skilled artisan to make crystal structures of other crystalline Hepatitis C virus helicases or co-complexes beyond those mentioned in the instant case where specific coordinates are disclosed. Due to the unpredictability and difficulty of crystallizing proteins, it is unlikely that one of skill in the art would be able to make another crystal relying solely on the information for the two crystals disclosed in the specification

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without undue experimentation. Also, the information provided in Examples 4 and 5, pages 49-50, does not sufficiently enable a skilled artisan to make compositions comprising crystalline Hepatitis C virus helicase as no specific chemical entities or ligands were mentioned. Again, due to the unpredictability in the art, a skilled artisan could not reasonably expect to make such co-crystalline complexes based on generic guidelines without undue experimentation.

Applicants did not provide arguments or any reasoning as to why the above rejection would be considered improper. Therefore their submission regarding the lack of enablement rejection is found unpersuasive and the rejection is maintained.

LACK OF WRITTEN DESCRIPTION

Claims 42 and 49-61 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time of the invention was filed, had possession of the claimed invention.

Claims 42 and 49-61 are directed to crystalline Hepatitis C virus helicases and compositions comprising the same. There is no disclosure regarding any crystals other than the tetragonal crystal having unit cell dimensions of $a = b = 109 \text{ \AA} \pm 3 \text{ \AA}$; $c = 84 \text{ \AA} \pm 2 \text{ \AA}$; $\alpha = \beta = \gamma = 90^\circ$; and space group $P4_1$ as well as the orthorhombic crystal having unit cell dimensions of $a = 66 \text{ \AA} \pm 2 \text{ \AA}$; $b = 110 \text{ \AA} \pm 3 \text{ \AA}$; $c = 64 \text{ \AA} \pm 2 \text{ \AA}$; $\alpha = \beta = \gamma = 90^\circ$; and space group $P2_12_12_1$. Claims 42, 49-52, and 58-61 do not appear to be limited to any particular unit cell dimensions. There is written support for particular tetragonal and orthorhombic crystals, but not for the broadly encompassed non-tetragonal and non-orthorhombic crystals as stated in with the broad term

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“crystal” in claims 53-57. Open claim language “comprising” in claims 53 and 54 suggests impurities or other material within the actual crystals that would more than likely affect the overall structure of the crystals and disrupt the tetragonal and orthorhombic structure of crystals in the invention. Amending claim language from “comprising” to “consisting essentially of” would nullify the rejection of claims 53 and 54, such that it is clear that the overall crystal structure is not disrupted. Claims 42, 49-54, and 58-61 broadly encompass crystals beyond the tetragonal and orthorhombic crystals, as described above, which do not meet the written description provision of 35 USC 112, first paragraph. Applicants have not sufficiently described these other crystals and compositions in such full, clear, and concise terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

The specification discloses SEQ ID NO: 1 which corresponds to an amino acid sequence of Hepatitis C virus helicase. SEQ ID NO: 1 meets the written description provisions of 35 USC 112, first paragraph. However, due to the facts that “having” (claim 42) and “comprising” (claims 50 and 51) are open claim language which may contain the entire sequence plus additional unspecified sequence, these claims are directed to encompass amino acid sequences other than SEQ ID NO: 1 which do not meet the written description provision of 35 USC 112, first paragraph. The specification provides insufficient written description to support the genus encompassed by the claim.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed*." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

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With the exception of SEQ ID NO: 1, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides and/or proteins, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

...To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." *Lockwood v. American Airlines, Inc.*, 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); *In re Gosteli*, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." *Lockwood*, 107 F.3d at 1572, 41 USPQ2d at 1966.

Therefore, only SEQ ID NO: 1 and the specifically mentioned crystals, but not the full breadth of the claims 42 and 49-61 meet the written description provision of 35 USC 112, first paragraph. The species specifically disclosed are not representative of the genus because the genus is highly variant. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.)

Applicants state that claim 51 has been amended to recite the crystal effectively diffracts x-rays to a resolution of 1.5 angstroms to 3 angstroms. This is found unpersuasive in overcoming the 35 USC 112, first paragraph rejections as the claim encompasses other crystals besides those specifically enabled and supported in the specification (see previous FINAL action,

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mailed 12/9/03, pages 4-8) through the use of open claim language "comprising" without mentioning the specific unit cell dimensions of the crystal to be claimed.

Applicants state that claims 42, 49, 50, and 52 have been amended to recite the crystal effectively diffracts x-rays to a resolution of 1.5 angstroms to 3 angstroms. Applicants also note the claims recite SEQ ID NO: 1. This is found unpersuasive in overcoming the 35 USC 112, first paragraph rejections as the claims encompass other crystals besides those specifically enabled and supported in the specification (see previous FINAL action, mailed 12/9/03, pages 4-8) without mentioning the specific unit cell dimensions of the crystal to be claimed.

Applicants state that claims 58 and 59 have been amended to recite SEQ ID NO: 1. This is found unpersuasive in overcoming the lack of written description rejection as the claims encompass other crystals besides those specifically enabled and supported in the specification (see previous FINAL action, mailed 12/9/03, pages 4-8) without mentioning the specific unit cell dimensions of the crystal to be claimed.

Request for Rejoinder

The request for rejoinder will occur if the product claims become allowable.

Conclusion

Claims 38-41 and 43 are allowable.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the

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Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR §1.6(d)). The CM1 Fax Center number is (703) 872-9306.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carolyn Smith, whose telephone number is (571) 272-0721. The examiner can normally be reached Monday through Thursday from 8 A.M. to 6:30 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Woodward, can be reached on (571) 272-0722.

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instruments Examiner Tina Plunkett whose telephone number is (571) 272-0549.

June 2, 2004


ARDIN H. MARSCHEL
PRIMARY EXAMINER 4/1/04